CORONARY INSUFFICIENCY: OBSERVATIONS ON DIAGNOSIS AND TREATMENT*

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CORONARY insufficiency is a functional disorder, not dependent upon any specific anatomic lesions for its occurrence. It may be defined as that condition in which the coronary arteries deliver less blood than is required for the effective performance of the heart. The disproportion between supply and demand can be brought about by a number of different factors which either diminish coronary flow or increase cardiac work. Its commonest cause is disease of the coronary arteries. Its two most important effects are anoxia and ischemia of the heart muscle. According to the current concept acute, local anoxia is the chief cause of cardiac pain. Prolonged ischemia, in the sense of a permanent reduction in coronary flow, may induce fibrosis of the heart muscle, cardiac hypertrophy and, eventually, congestive failure. In this discussion cardiac infarction and congestive failure will not be considered. Attention will be focussed on the paroxysmal type of pain to which the term "anginal" has been applied.

CAUSES OF CORONARY INSUFFICIENCY

Before proceeding to a consideration of diagnosis and treatment, it is necessary to have clearly in mind the various clinical conditions which may result in an inadequate coronary flow. Among the most important are:

1. Diseases of the coronary arteries.
    A. Atherosclerosis. This may be
        a. Slight, with patchy intimal change and loss of elasticity.
        b. Marked, with calcification and narrowing.

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c. Occlusive, as a result of obliteration of the lumen by the sclerotic process or due to the formation of a thrombus.

B. Syphilis of the aorta, with stenosis of one coronary orifice, or of both. The specific process is limited to the first 3 or 4 mm. of the coronary arteries.

C. Embolism. This occurs infrequently; the two most common sources of emboli are bacterial vegetations on the mitral or aortic valve, or a thrombus covering a sclerotic plaque at the root of the aorta.

D. Rheumatic fever, with involvement of the coronary arterial walls and, occasionally, thrombus formation.

E. Periarteritis nodosa, a relatively rare condition, but one in which coronary involvement is not uncommon.

2. Aortic valvular disease. In aortic stenosis, less frequently in aortic insufficiency, the coronary blood flow may be diminished. In free aortic regurgitation this is believed to be due to the lowered diastolic pressure.
3. Anemia. The heart suffers from anoxemia along with the rest of the body.
4. Paroxysmal tachycardia. The rapid rate may call for a greater coronary flow than can be delivered.
5. Hyperthyroidism. The increased metabolic demands of the body require a faster velocity of blood flow and an augmentation of volume output by the heart. Cardiac work may exceed coronary reserve.
6. Combined states. For example, a person with coronary sclerosis will experience pain more readily if marked anemia is present than if the oxygen-carrying capacity of the blood is normal. Ischemia and anemia complement one another in causing anoxemia.

It is thus evident that pain of coronary origin may result from systemic disorders as well as from those which are primarily cardiac. But there are other conditions which, on occasion, induce pain in the chest, and simulate that due to coronary insufficiency. Among these are:

1. Acute, serofibrinous pericarditis.
2. Aneurysm of the thoracic aorta.
3. Cholelithiasis.

4. Duodenal ulcer.
5. Poisoning by coffee, tea or tobacco.
6. Intercostal neuralgia or myalgia.
7. Psychoneurotic states.

The aim of diagnosis is to determine the etiology, to define the anatomic lesions and to estimate the degree of functional impairment. No attempt will be made here to outline a complete diagnostic survey or to give a full account of therapeutic procedure. These remarks deal with scattered observations, assembled over a period of years and concerned chiefly with cardiac pain due to coronary sclerosis.

Diagnosis

In no other condition is the patient's account of his discomfort of greater importance. Often this suffices for diagnosis. So, it is essential that the physician who is responsible for the management of the case should himself take the history. A story obtained by a colleague, no matter how competent he may be, cannot convey the same impression as that obtained from a personal interview. From this contact is often obtained the key to the entire situation. There is established an understanding and a relationship which is never gained through an intermediary. Furthermore, pain is so frequently the only evidence of coronary disease that its precise description by the sufferer must be heard in order that its significance can be appraised and its implications analyzed.

The physical examination may be entirely negative. The heart is often not enlarged, the sounds are normal and the blood pressure is not elevated. The retinal and peripheral vessels may show no sclerosis. Of positive value, though in no sense etiologically specific, are cardiac enlargement and weak heart sounds. Sometimes the first sound at the apex is split; a diastolic gallop may be heard. The presence of hypertension is not, of itself, a decisive feature.

The same viewpoint obtains with respect to the electrocardiogram. A normal record does not rule out the presence of advanced and, sometimes, serious coronary insufficiency. A case has previously been reported,[1] in which a patient with a typical history of anginal pain presented no objective signs of cardiac disease. The four-lead electrocardiogram showed no characteristic changes in T waves, RS-T segments or in conduction. Yet within twenty-four hours, this man of 49 died suddenly at the breakfast table. The presence of abnormalities in the elec-

trocardiogram is, however, of great help in furnishing positive evidence of myocardial damage.

Not infrequently, it is difficult to decide whether a person complaining of pain in the chest is suffering from coronary insufficiency or from one of the conditions simulating it, having its origin either within the thorax or below the diaphragm. To aid in differentiation and in detecting latent coronary insufficiency, the "anoxemia test" has been devised and, in our hands, has proved to be of practical value.[2, 3]

In principle, this test consists of permitting the patient to breathe a mixture of 10 per cent oxygen and 90 per cent nitrogen for 20 minutes, or until cardiac pain appears. Measurements of electrocardiograms taken at intervals during this period reveal, in patients with a diminished coronary reserve, characteristic changes which are not observed in the presence of an adequate coronary blood flow. A positive test may thus be regarded as a sign of coronary insufficiency; but a negative test does not exclude the presence of disease of the coronary arteries. The occurrence of pain during a negative test, that is, one in which no electrocardiographic changes have occurred, affords *presumptive* evidence of a diminished coronary reserve.[4] It is of particular significance when the pain appears during the first 10 minutes of induced anoxemia. Patients experiencing painful discomfort during a negative test should be carefully observed for further signs of coronary disease and managed conservatively.

The criteria of a positive reaction have been evolved after experience with the performance of the test more than 1100 times in over 500 persons, some with normal hearts, others with cardiac disease. They are as follows:

1. The arithmetical sum of the RS-T deviations in all four leads (I, II, III, and IVF) totals 3 mm. or more.

2. There is partial or complete reversal of the direction of T in Lead I, accompanied by an RS-T deviation of 1 mm. or more, in this lead.

3. There is complete reversal of the direction of T in Lead IVF, regardless of RS-T deviation.

4. There is partial reversal of the direction of T in Lead IVF, accompanied by an RS-T deviation of 1 mm. or more, in this lead. Of the four, this criterion is of the least value. It rarely occurs alone, and has been noted twice in borderline cases.[5] If further experience confirms these observations, it will be discarded.

The anoxemia test is simple and safe. Unpleasant reactions have been observed, such as vasovagal attacks, panic, loss of consciousness and dyspnea. These were relatively uncommon and not serious. In the course of 4 years, there has been no evidence of permanent injury to a single patient, although the test has been performed in the same person as often as 20 times. Early in the work, pulmonary edema occurred 3 times. But if the test is not given to a patient with congestive heart failure, to one who has had an attack of cardiac infarction within 4 months or to the same patient twice within 24 hours, no grave accidents are to be anticipated. The percentage of oxygen in the gas mixture should be checked at frequent intervals to be sure that the proper concentration is being supplied.

The test has been helpful in the differential diagnosis of conditions producing pain in the chest. It has been employed to study, in patients, the effect of various drugs on the coronary circulation. It has been useful in following variations in the coronary reserve and so appraising the efficiency of the coronary circulation at the time of its performance.[4]

The following case record serves to illustrate the type of changes which are seen in the electrocardiogram when coronary insufficiency is present, and portrays graphically the increase in coronary reserve coincident with clinical improvement.

Case I. W. D., aged 48 years, foreman in a U. S. Post Office, was admitted to the hospital on March 18, 1939. He had been well until a week before, when he had a typical attack of coronary occlusion with cardiac infarction. During this week he had been attended by his own physician. He was transported by ambulance and arrived in good condition.

On admission, the rectal temperature was 100.4° F. The heart was a little enlarged. The rhythm was regular; the rate 64. The first sound at the apex was split. The blood pressure was 120/80. The leukocyte count was 7,880, with 75 per cent polymorphonuclears. The sedimentation rate was 45 mm. in one hour, and rose on the following day to 54 mm. The Kline test of the blood was negative. An electrocardiogram showed prolonged auriculoventricular conduction (the P-R interval measured 0.33 sec.). Other changes were characteristic of a posterior infarct.

The patient remained in the hospital for 5 weeks. The course was one of steady improvement, both clinically and in the form of the electrocardiogram. At the end of another 2 weeks (8 weeks after his attack)

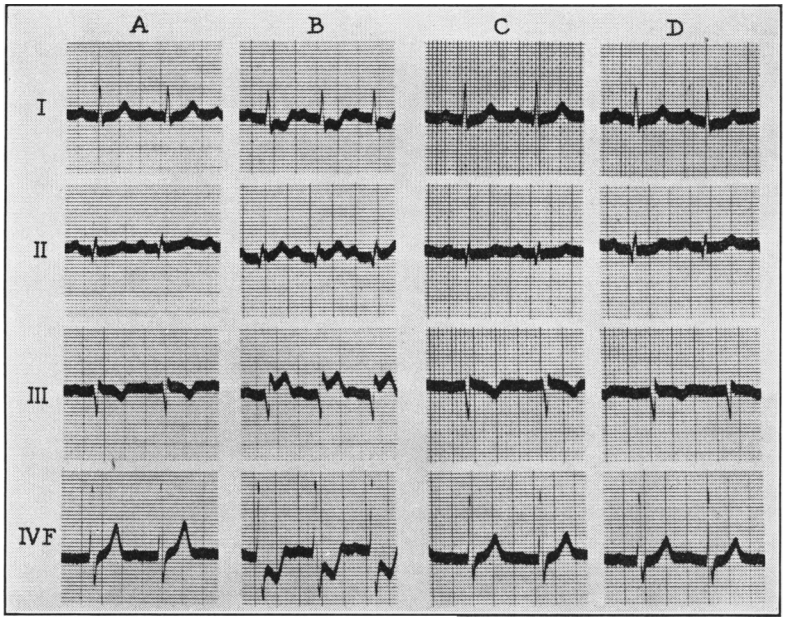

Fig. 1. *Case 1.* W. D., male, aged 48 years, foreman in Post Office. Coronary occlusion with myocardial infarction on March 11, 1939. Anoxemia test, at first positive, became negative.
Five months after attack. Working too hard and having frequent attacks of anginal pain. A—control. B—positive test: pain after 18 minutes; total RS-T deviation, 9.5 mm.; T wave reversal in Leads I and IVF.
Nine months after attack. Work lighter and nearer home. Rare attack; no nitroglycerine required. C—control. D—negative test; no pain during 20 minutes of anoxemia.

he returned to work, in spite of having been advised to extend his period of rest. When tired, he complained of aching in the left shoulder and arm. Subsequently he experienced cardiac pain on effort and in August, 1939 (5 months after the occlusion) was having frequent anginal attacks. An anoxemia test at this time was positive (Fig. 1. A, B).

He was then able to transfer to a Post Office nearer his home and was made a supervisor. The work was lighter and he improved. Nine months after the original attack, he was not taking nitroglycerine and could walk for 6 or 7 blocks before experiencing discomfort. The heart sounds were of good quality. The blood pressure was 120/72. The anoxemia test at this time was negative (Fig. 1. C, D).

The test does not furnish evidence which makes it possible to predict the future occurrence of coronary occlusion. Several patients have

suffered such attacks within a few months of the time that a negative test was found. On the other hand, patients with a positive reaction are more likely to have this complication than those in whom the reaction is negative. The test is therefore an index, within undefined limits, of the functional efficiency of the coronary circulation; but it yields no information as to the nature and extent of the pathologic lesions in the heart.

Treatment

Medical Measures. Any person who has pain in the region of the heart is alarmed. He thinks at once of a relative or friend who has died suddenly following a similar complaint and his first question is apt to be: "Have I angina pectoris?" He wants, above all, reassurance. It seems to me good practice, under these circumstances, to state at the outset that there is no disease such as angina; that this term means merely a painful or uncomfortable sensation in the chest, and that it will be our aim to discover the nature of the condition which lies at the basis of the discomfort.

These patients are worthy of the expenditure of much time on the part of the physician and attention to detail is necessary if therapy is to succeed. A carefully planned regimen, designed to save the heart from overwork, will aid in the establishment of a collateral circulation in the coronary bed. The intelligent use of nitroglycerine, not only for the relief of pain when this occurs, but prophylactically, when some necessary effort is anticipated, will prevent the occurrence of myocardial anoxia. There is evidence, both clinical and experimental,[6, 7] that repeated and prolonged impairment of the coronary blood flow causes minute focal necroses in the heart muscle and, in time, replacement fibrosis. The avoidance of painful attacks is, therefore, of therapeutic importance.

Of the various drugs which have been used in treatment, the xanthines have received most attention. There has been difference of opinion with respect to their efficacy as coronary dilators; and conflicting reports have appeared concerning their usefulness in lessening the frequency and intensity of anginal paroxysms. The changing conditions in the coronary circulation as a result of disease and the many external factors which may modify the clinical course of patients subject to attacks of cardiac pain, make difficult a just appraisal of the effect of medicinal remedies which exert their action over a long period of time.

For this reason, an objective test was applied to the problem in the form of induced anoxemia.[8,9] Changes in the form of the electrocardiogram were studied in patients with coronary sclerosis, before and after the administration of different members of the xanthine group. The time of appearance of pain during anoxemia was also observed and variations due to drugs were noted. In brief, it was found that various members of the xanthine group (aminophylline, theophylline with sodium acetate and theobromine with sodium acetate) in proper dosage, caused a decrease in the RS-T deviation of the four-lead electrocardiogram and prolonged the time of appearance of pain. These results were obtained by averaging the observations obtained in a group of patients and expressing the effects as a trend. This was necessary because not all patients respond favorably, as might be anticipated from the varying character of the coronary lesions in different hearts. In general, patients with less severe and less frequent attacks show a better therapeutic response than do those with more advanced coronary insufficiency. In our hands, aminophylline, because it is best tolerated by the digestive tract and does not require as large doses as some of the other members of the group, has proved the most satisfactory drug. It may be given in doses of 0.2 Gm. (3 grs.) three or four times daily. Enteric-coated tablets are available and may be prescribed for those who report digestive disturbances.

Recent studies made in our laboratory indicate that the duration of action of this drug, when taken by mouth, lasts only for a few hours. This observation suggests that perhaps smaller doses, taken at shorter intervals, might exert a more beneficial action. Work designed to indicate the most effective method of administration is now in progress. It is our present opinion that in certain cases the xanthines, because they dilate the coronary arteries, bring about symptomatic improvement. Whether, if taken for weeks or months, they aid in promoting a collateral circulation, cannot be decided on the basis of the evidence now at hand.

Surgical Procedures. Most patients with cardiac pain respond favorably, in some degree, to medical therapy. But there are those who suffer so intensely that they question the desirability of living. Fortunately, they do not form a large group. They welcome with enthusiasm any form of therapy which offers a reasonable hope of relief.

Of the various operative measures which have been suggested, only one will be considered at this time. Cervical sympathectomy and total

removal of the thyroid gland have not stood the test of trial and have been almost universally discarded. Section of the dorsal nerve roots, performed on a few selected cases, has been successful; but it is a major operation requiring laminectomy and presents a real hazard for the patient with advanced coronary disease. The operation for the formation of a new blood supply to the heart, as devised by Beck,[10, 11] holds out real promise, particularly if the technique can be simplified.

There remains for discussion paravertebral block with alcohol. This was first suggested by Swetlow in 1926[12] and has been done in various clinics, both in this country and abroad. The largest series, 62 cases, has been reported by J. C. White of Boston.[13] My own experience, recently published in collaboration with R. L. Moore, is based on observations in 45 patients.[14] Since our results and those at the Massachusetts General Hospital are comparable and similar, I will confine my comments to the material with which I am familiar.

Alcohol block is a simple technical maneuver; but it requires an operator familiar with the landmarks, skilled in their use and deft because of constant practice. The effectiveness of the injections depends entirely upon the accuracy with which the ganglia and rami communicantes are infiltrated. Our results may be summarized as follows:

Of 40 patients subjected to final analysis, 77.5 per cent experienced varying degrees of improvement; no relief was obtained in 22.5 per cent. In 47.5 per cent of the total number benefited, improvement was permanent to the time of the last follow-up examination, which in 2 cases was more than 9 years. In 40 per cent, relief was marked, in 5 per cent it was moderate and in 2.5 per cent it was slight. Temporary relief was obtained in 30 per cent. This was marked in 15 per cent, and moderate in 15 per cent. In short, there is a 75 per cent chance of relief; and if relief is obtained, there is an even chance that it will be permanent. Neither the duration of symptoms nor a previous history of coronary occlusion nor the degree of incapacity prior to injection appeared to influence the outcome. The postoperative appearance of Horner's syndrome was not essential to a successful result.

In none of our cases was relief complete. Even when a result was obtained which was satisfactory to the patient, some form of discomfort persisted, to act as a warning signal. There were sometimes actual twinges of pain, of less intensity than before injection, or a sense of pressure beneath the sternum. In several cases, mild dyspnea or a sinking

sensation in the epigastrium was substituted for pain.

Almost invariably (in 38 of 40 patients) painful intercostal neuritis was observed after the injection. This was severe in only 3 instances. It lasted from 2 weeks to 3 months but eventually always disappeared. Whereas it was a cause of complaint, the relief of cardiac pain, when obtained, more than compensated for discomfort. In 5 cases, a small pleural effusion developed which was always absorbed within a week. Pneumothorax, reported by others, was not observed. Increased temperatures, from 99 to 104° F., occurred in 25 patients; fever never lasted more than 4 days unless complicated by pleural effusion. There was no operative mortality.

Why, in some cases, relief should be temporary and in others permanent, has been explained by the recent experimental observations of Merrick.[15] He found that in cats, when a ganglion was infiltrated with alcohol, permanent block was produced to all regions innervated by the postganglionic fibers taking origin from it. This occurred because the alcohol killed the ganglion cells. When the rami communicantes alone were infiltrated, only a temporary block was produced; for regenerating fibers penetrated fairly early through the connective tissue scar formed at the site of injection. Partial block in patients is probably due to incomplete destruction of the ganglion cells or rami.

There is some reason to believe that abolishing or relieving cardiac pain not only affords symptomatic relief but has an effect on the coronary circulation and so on the heart muscle. A group of Toronto investigators,[16, 17] working with conscious dogs, observed that when the heart was denervated, the mortality following sudden occlusion of a coronary branch was materially less than in the intact animal. These experiments were regarded as indicating that, by preventing afferent impulses from reaching the vasoconstrictor center, reflex spasm of collateral coronary arteries was prevented. It was apparent also that sympathetic denervation rendered the myocardium less susceptible to the onset of ventricular fibrillation. Clinical and necropsy observations support those made in the physiological laboratory.[18] Of 376 patients who died of coronary sclerosis and thrombosis and were examined post mortem at the Presbyterian Hospital, 52 died suddenly. In the group with pain, death was sudden in 27.5 per cent, and in the group without pain in only 9.1 per cent. Regardless of the extent and character of the coronary lesions, the presence of pain tripled the incidence of sudden death.

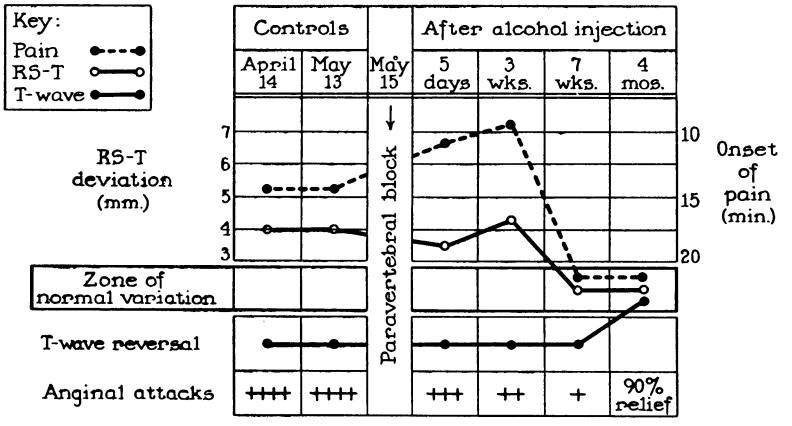

Fig. 2. *Case 2.* O. F., male, aged 53 years, automobile salesman. Anginal pain for five years; unable to work for the past three because of disability. Anoxemia test positive prior to paravertebral alcohol block. Four months after injection, coincident with clinical improvement, test became negative.

In 2 of our cases, changes in the form of the electrocardiogram occurred shortly after alcohol block. The alterations in the complexes were in the direction of normal and suggested an improvement in the coronary blood flow.[14] Observations with the aid of the "anoxemia test," made before and after injection, have shown in the one patient in which this has been done, remarkable improvement in the coronary reserve, coincident with clinical improvement (Fig. 2). A brief abstract of the clinical record follows.

Case II. O. F., aged 53 years, a male, automobile salesman, for 5 years had been having typical anginal pains radiating to the left arm. Disability became progressively more marked and for the past 3 years he was unable to work. He also had a feeling of substernal pressure and dyspnea after meals. He was unusually intelligent and coöperative.

Examination showed no cardiac enlargement, either on percussion or in the teleroentgenogram. The heart sounds were of fair quality. There was no gallop; a blowing systolic murmur was heard at the apex. The blood pressure was 140/82. The electrocardiogram showed regular sinus rhythm with a Q wave present in leads one and two. There was no defect in conduction and the T waves were normal. There was no anemia. The Kline test of the blood was negative.

The anoxemia test, done on a number of occasions, was positive.

Two controls, obtained at an interval of a month, were identical (Fig. 2). They show the occurrence of pain at the end of 14 minutes, a total RS-T deviation of 4 mm. and significant reversal in the direction of the T waves.

Paravertebral alcohol block was done on May 15, 1941 by Dr. R. L. Moore. Injections were made in the region of the first five dorsal ganglia. Horner's syndrome developed. There was moderate pain from intercostal neuritis, which disappeared in the course of 2 months. At the end of 4 months, he estimated the degree of improvement at 90 per cent. He was able to walk 2 or 3 miles without discomfort, except after a heavy meal. He had not used nitroglycerin since the operation and stated that dyspnea was gone. The blood pressure was 140/80. The form of the control electrocardiogram was unchanged. The anoxemia test at this time was negative.

In view of these various pieces of evidence, it appears that interruption of the sensory pathways, in certain cases, may diminish or abolish spasm in the coronary bed. This is a desirable effect, tending to promote a more adequate collateral flow in unaffected vessels. As has been previously suggested, earlier relief of pain in patients with coronary sclerosis might be expected to influence the course of the disease in a favorable manner. But in the more advanced cases, even when the result was good, unilateral alcohol block did not prevent the later occurrence of coronary occlusion or of sudden death.

In conclusion, I would like to leave with you this thought. The patient with recurring cardiac pain suffers usually from a progressive, disabling disease. Yet in some cases there is a remarkable and unexpected turn for the better; in others, the increase in the symptoms of coronary insufficiency is gradual and the degree of disability is slight. The physician can bring both aid and comfort. He is sometimes discouraged when improvement is slow and his therapeutic efforts appear to be ineffectual. He will find it helpful, under such circumstances, to keep in mind three master words—resourcefulness, patience and optimism. Of these, the most important to both doctor and patient is optimism.

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